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This progress report consists of two parts reviewing separately the experimental and theoretical studies carried out.

Part I -- Experimental -- In an effort to characterize minimum cell size we have shifted attention to the problem of minimum information content. An extensive effort has been made to measure genome size of a number of mycoplasma species in order to find the smallest genome on which to carry out further work.

a) Mycoplasma hominis H39. The genome of this cell has been spread to the method of Kleinschmitt and subsequently picked up on grids shadowed and examined in the electron microscope. Three thousand displays of DNA were examined. Six circles and one replicating circle were obtained. The genome size is the order of 250 microns or 500×10^6 daltons. This is the smallest reported genome for any cell and limits the genetic information to about 600 cistrons.

b) Mycoplasma arthritidis. The genome of the cell is currently under study and appears to be the same size as the H 39 strain.

c) Mycoplasma laidlawii P. The genome is clearly larger than H39 and by microscopy appears to be about 800×10^6 daltons. The size has been independently measured by the method of Cairns using titrated thymidine and radioautography. This also yields a length of 800 microns.

d) Measurements are in progress on Mycoplasma gallisepticum A5969 and the KID strain (possibly M. agalactia kid.).

Part II -- Theoretical -- An extensive examination is in progress of the thermodynamic limitations underlying the living processes. The first part of this work is attached.

CHAPTER I

The purpose of this book is to discuss and present evidence for the general thesis that <u>the flow of energy through a system acts to organize that system</u>. The motivation for this approach is biological and has its origins in an attempt to find a physical rationale for the extremely high degree of molecular order encountered in living systems. From the study of energy flow in a number of simple model systems, we shall attempt to demonstrate that the evolution of molecular order follows from known principles of present day physics and does not require the introduction of new laws. In addition, we shall note that the biological utility of existing theoretical physical chemical concepts becomes manifest when we turn from the restrictions of equilibrium thermodynamics and concentrate attention on the rich possibilities of non equilibrium and steady state theory. Even equilibrium theory can acquire more biological meaning when we consider geological time scales and therefore allow an appreciably wider range of accessible states.

It is, thus, the plan of this work to examine certain aspects of biology in terms of the concepts of thermodynamics, statistical mechanics and kinetic theory. Such an examination will, we believe, lead to a much closer relation between biology and physics and will make clearer the sense in which biology can be viewed as a special branch of physics.

By way of historical introduction, we may point out that it is now over one hundred years since the introduction of the theory of evolution in biology and the second law of thermodynamics in physics. Each of these principles has been a unifying and heuristic theory within its own science. Yet, the relationship of biology to physics has sensed a slight antagonism between evolution and increasing entropy.

Biological evolution involves a hierarchical ascendency to more and more complex forms of living systems. The second law of thermodynamics asserts that the universe or any isolated section of the universe that we choose to consider is tending toward maximum entropy. Consideration of statistical mechanics as well as kinetic theory make it clear that maximum entropy involves maximum disorder consistent with the constraints of the system. Thus, when we think of evolution within the context of the Bolzmann H theorem, we think of evolution to more and more disordered states of the system.

The resolution of this apparent divergence between a biological and a physical theory is the realization that the second law of thermodynamics applies to systems that are approaching equilibrium while the surface of the earth, the matrix of biological evolution, belongs to a different class of physical systems. Equilibrium systems require either isolation (adiabatic systems) or contact with a single fixed reservoir (isothermal systems). Most real physical systems are of another sort; they are in contact with

more than one reservoir some of which may be regarded as sources and some of which may be regarded as sinks. The description of these systems requires the consideration of the flow of either matter and or energy from the sources through the systems of interest to the sinks.

Steady state systems constitute a special case where the sources and sinks are fixed so that as the system ages, the flows from sources to sinks become constant and the local intensive parameters of the systems (temperature, concentration, pressure, etc.) become time independent. In non equilibrium systems, the exact significance of the intensive parameters is not always clear, especially in cases far from equilibrium. In any case, the macroscopically measurable parameters become time independent in the steady state.

The difference between equilibrium and steady state systems is that in the latter, there is a continuous net flow of either matter or energy through the system from and to external reservoirs. The steady state as well as other non equilibrium systems are not characterized by entropy maxima and need not be considered within the narrow confines of the second law of thermodynamics. A body of theory has grown up in recent years attempting to characterize the precise formal requirements and conditions of the steady state.

(1, 2, 3) Works in this field have been termed steady state thermodynamics, non equilibrium thermodynamics, irreversible thermodynamics, or just thermodynamics to those who would apply the term

thermostatics to traditional equilibrium theory.

Much of this monograph is an attempt to characterize non equilibrium states and to show how they acquire properties that are very different from those that might be expected in the equilibrium state. These properties in turn have important implications for biology. The surface of the earth clearly belongs to the class of systems in contact with a source and a sink. The source is, of course, the sun which is constantly irradiating the earth with a flux of photons. The sink is outer space. The night side of the earth radiates infra-red. The significance of this process will be clear to those who have experienced nightfall on a high mountain or on the desert and have noticed the rapidity of the temperature drop. The earth as a whole is in approximately a steady state with respect to radiation: the flux of solar radiation is just balanced by the loss of energy to outer space.

To sum up our general argument, we note that in order to study evolution or increasing organization as a physical process, we must depart from equilibrium considerations and examine the molecular physics of steady state and other non equilibrium systems. This is not to assert that tradition equilibrium thermodynamics has no role in biology; the use of calorimetric and thermochemical concepts has already been of great utility in biochemistry and ecology. However, it is the theme of this chapter that non equilibrium studies will lend considerable insight into the evolution and functioning of living systems.

To provide a background for examining the energy flow principle,

we shall first consider a particular model system which is designed to

illustrate some of the limitations of equilibrium systems and indicate the

special areas of inquiry necessary to overcome these limitations and

establish a biophysics, a theory of biology rooted in physics.

Consider then a system which has the same atomic composition and

volume as a given living cell and is in contact with an isothermal reservoir

at some appropriate temperature. At equilibrium what is the probability

that this system will, in fact, be a living cell? While we must recognize at

the onset that any attempts to answer this type of question in detail are at

the moment impossible, none the less, useful insights can be gained from a

study of the question and certain limiting statements that can be made. First,

we can give the question a less abstract formulation by the following Gedanken

experiment. Suppose, we were to grow up a very large batch of cells of a

bacterium such as Escherichia coli. We, then, centrifuge the cells into a

tightly packed pellet of volume V containing N cells, transfer the pellet into

a container of fixed volume V and raise the temperature to some very high

value (the order of $10,000^o$ C) so as to destroy any traces of the original

chemical state of the system. Now, slowly cool the system to 300   and

allow it to age indefinitely at this temperature. The system may now be

considered as a group of subsystems of volume v =V/N, indeed it constitutes

a grand canonical ensemble* of such sub-systems. If the ensemble were

infinite, members   would represent all possible physical states of the

sub-systems consistent with the constraints. It will be more convenient in subsequent considerations to use a canonical ensemble rather than a grand canonical ensemble. This can be achieved in our Gedanken experiment by subdividing the system into sub-systems of volume V such that all sub-systems have the same atomic composition. The sub-systems are then separated by walls impermeable to matter, but capable of conducting heat. Among the possible states of the system, some must correspond to living

cells. This can be taken as proven since the initial bacterial cells represent

systems of the same volume and atomic composition and temperature as the

final members of the ensemble. As the initial cells were alive, this state is

clearly a possible one for members of the canonical ensemble; although,

as we shall see, such states have exceedingly small probabilities. Each

possible state of the ensemble members may be designated the ith state

having energy ϵ_i. The probability of the system being in the ith state at

equilibrium is then:

$$1\text{-}1 \qquad p_i = \frac{e^{-\epsilon_i / k_b T}}{\sum e^{-\epsilon_j / k_b T}}$$

Since the Ei represent energy states, rather than energy levels, we need not

include a degeneracy term. (See S. T. Chapter I). We now introduce a

biological delta function $\delta_{i L}$. This function has the value one if the

ith state is living and the value 0 if it is non living. The probability of a

given member of the ensemble being in the living state is then:

$$1\text{-}2 \qquad p_L = \frac{\sum_i \delta_{i L} e^{-\epsilon_i / k_b T}}{\sum e^{-\epsilon_j / k_b T}}$$

At this point, we can place an upper bound on p_L by applying our know-

ledge of the chemical bonds found in actual living systems compared to the

bonds found in the normal equilibrium state. We will, then, find that p_L

must equal zero for all $\epsilon_i < \epsilon_m$, where ϵ_m represents the minimum

bond energy above the ground state energy for living systems. We will, then,

note:

1-3
$$p_{L\ max} = \frac{\sum^{m} e^{-\epsilon_i / kT}}{\sum_{1}^{m} e^{-\epsilon_j / kT}}$$

Since reasonable estimates of ϵ_m are possible (p_L) max may be calculated,

or at least a crude estimate may be obtained.

The preceding paragraph involves some assumptions which require

discussion. First, we have assumed a principle, that is an empirical

generalization from biochemistry, that all living systems have a large number

of chemical features in common. To note a few, consider the amino acids of

proteins, the nucleotides, intermediate phosphate compounds and sugars. The

distribution of covalent bonds in a living system is, thus, a characteristic

feature of that system as is the heat of formation of those bonds. From a

thermodynamic argument, it is possible to compute the heat of formation of

a group of biochemical compounds relative to the lowest energy state possible

to the same atomic composition volume and temperature; hence, on the basis

of gross molecular composition, we can estimate the energy difference between

biological systems and their corresponding ground states. We shall do this

from different points of view in Chapters III and IV. Since the biochemistry

of terrestrial life appears to be so ubiquitous, this energy difference is a

characteristic parameter of living systems as we know them.

In Chapter III, we shall set up a model system that will permit the

calculation of $p_L$max. At the moment, we may anticipate the results of that

calculation which shows that $p_L$max is the order of magnitude of 10^{-10} ^{12}.

The reason for p max having such an infinitesmally small value, is that a

living cell represents a configuration showing a very large amount of energy

as configurational or electronic energy relative to the amount of thermal

energy when compared with the equilibrium system. The living state has a

very unlikely distribution of covalent bonds compared to equilibrium state

either at the same total energy or at the same temperature. The living state

might be regarded as having a very high electronic temperature relative to

its normal thermodynamic temperature. It is chemically at a high potential.

Here, we might anticipate one of our general conclusions. Living systems

are at a high electronic energy because the absorption of solar photons

produces high potential compounds. In the subsequent degradation of this

energy to heat a number of other high energy compounds are produced along

the way with the general result that the biosphere is at a relatively high

level of potential energy when compared to the energetic ground state.

A simple example will demonstrate this property and anticipate

the application of energy flow to such systems. Consider a simple chemical

reaction of the type represented by a potential energy diagram of the type

shown in Figure 1-1. In discussing chemical reactions, we will employ the formalism of absolute reaction rate theory (7). Assume that we have a reaction vessel with A and B in an isothermal isobaric bath of temperature T.

At equilibrium

1-4
$$\frac{[B]}{[A]} = e^{-\Delta F/RT}$$

where ΔF is the Gibbs Free energy change of the reaction and R is the gas constant. The overall reaction represents a balance of forward reaction

proceeding at a rate $[A]\left(\frac{kT}{h}\right) e^{-\Delta F_f^{\ddagger}/RT}$ and a back reaction

proceeding at a rate $[B]\left(\frac{kT}{h}\right) e^{-\Delta F_b^{\ddagger}/RT}$.

The $\Delta F^{\ddagger}$'s are activation free energies, h is Planck's constant and k is the Boltzmann constant.

Next irradiate the system with photons of appropriate energy to yield a photochemical transition from A to B. Assume the flux is G photons per second and the geometry of the vessel is such that they are all absorbed. Assume that the back reaction proceeds by collisions of the second kind and involves no radiation but a conversion to thermal energy. The system will eventually reach a steady state, heat will be transferred to the reservoir and the following conditions will obtain.

1-5
$$G(h\nu) = a(T' - T)$$

ν is the frequency of the radiation, a the thermal transfer coefficient from the vessel to the reservoir and T' is the steady state temperature of the

irradiated system.

This equation expresses the condition of the steady state that the amount of energy flowing into the system is to equal the amount leaving the system. The forward and back reactions now have rates of

$$[A'] \frac{kT'}{h} e^{-\frac{\Delta F_1^{\ddagger}}{RT'}} + G \qquad \text{forward and}$$

$$[B'] \frac{kT'}{h} e^{-\frac{\Delta F_2^{\ddagger}}{RT}} \qquad \text{back}$$

In the steady state these are equal, and

1-6 $\qquad \dfrac{[B']}{[A']} = \dfrac{k_1 M + G}{k_2 M - G}$ 　　where M is the total amount

of A and B and k_1 and k_2 are

rate constants of the form $\dfrac{kT}{h} e^{-\frac{\Delta F^{\ddagger}}{RT}}$

Substitute G = g M where g is the

flow of photons per molecule

1-7 $\qquad \dfrac{[B']}{[A']} = \dfrac{k_1(T') + g}{k_2(T') - g}$

The equilibrium value at temperature T' in the absence of irradiation would

have been $\qquad k_1(T') / k_2(T') = e^{-\frac{\Delta F}{RT'}}$

The actual value is higher than this and corresponds to an effective electronic

temperature T'' which can be obtained from

1-8 $\qquad \dfrac{[B']}{[A']} = \dfrac{\frac{kT'}{h} e^{-\frac{\Delta F_1^{\ddagger}}{RT'}} + g}{\frac{kT'}{h} e^{-\frac{\Delta F_2^{\ddagger}}{RT'}} - g} = e^{-\frac{\Delta F}{RT''}}$

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The chemical state of the steady state system corresponds to the chemical state of an equilibrium system at a higher temperature. It is this feature that is characteristic of biological systems.

In systems of any degree of complexity, it is not possible to calculate a single T'' which will describe the energy distribution of the system. The concept is, however, clear if we consider the usual approximation that the energy of a system may be broken up into electronic, translational, rotational and vibrational.

$$1\text{-}9 \qquad \epsilon = \epsilon_e + \epsilon_T + \epsilon_r + \epsilon_v$$

In the chemical systems we are discussing, energy will be distributed among the possible energy levels in a Maxwell-Boltzmann distribution for translation, rotation and vibration. This distribution will define a temperature of the system and will be the measured temperature by most kinds of thermometers. Energy will be distributed in the electronic levels in such a way that the upper levels will be more populated than would be expected for a Maxwell-Boltzmann distribution at the system temperature. This is all that we shall generally imply by the concept of elevated electronic temperatures.

Note that in the previous model system, the condition of high electronic energy was maintained by a flow of energy through the system. This accords with our thesis about energy flow and will subsequently be

developed as a more general case.

Next, let us return the number $10^{-10^{12}}$ which requires some discussion as many people are not familiar with dealing with such infinitesimally small numbers. The number may be written $10^{-1000000000000}$ or as a normal decimal, it may be written as a decimal point followed by 999,999, 999,999 zeros followed by a 1. The number occurred as the maximum probability of a given ensemble member being alive. We may then ask the question, supposing we have an ensemble of A members and we sample at the rate of B times per second for C seconds, what will be the probability of a living member having occurred once? This will be p_L ABC. To place our argument in the context of terrestial biology, let us assume the maximum possible values of A, B, and C for the surface of the earth.

(a) A max = 10^{100} This is the estimated number of atoms in the universe and must,therefore, represent an upper limit to the numbers of members of the ensemble.

(b) B max = $10 \frac{16}{sec}$ Since we are dealing with atomic processes, sampling times cannot be appreciable shorter than times for atomic processes which have a lower limit of about 10^{-16} seconds.

(c) C max = 10^{18} sec. Assume the age of the universe is ten billion years, which appears to be an upper limit from current estimates.

A max B max C max = 10^{134}

Note, however, that

p max A max B max C max $\widetilde{=}$ p max

$$10^{-(10^{12}-133)} \cong 10^{-10^{12}}$$

Since $133 < < 10^{12}$

When we encounter numbers of such a small size as p max, no amount of

ordinary manipulation or arguing about the age of the universe of the size

of the system can suffice to make it plausible that such a fluctuation would

have occurred in an equilibrium system. It is always possible to argue that

any unique event would have occurred. This is really outside of the range of

probabilistic considerations; and, in a sense, lies outside of science. We

shall subsequently show that it is not necessary to invoke such arguments to

explain biological organization. We may sum up this argument by stating

that on energy considerations alone, the possibility of living cell occurring

in an equilibrium ensemble is vanishingly small.

It is important to reiterate the point made in the last paragraph as

a number of otherwise sophisticated authors on the origin of life have

missed the significance of vanishingly small probabilities. They have

assumed that the final probability will be reasonably large by virtue of the

size and age of the system. The last paragraph shows that this is not so:

calculable values of the probability of spontaneous origin are so low that

the final probabilities are still vanishingly small.

The concept of p_i may be generalized to give us a measure of order that is applicable to abiotic systems as well as living systems. Consider any non equilibrium state of a system for which we can define a set of macroscopic or microscopic properties. Then, consider the same system isolated by rigid walls and allowed to equilibrate with a reservoir which is at the same temperature as the initial system*. If we consdier the equilibrium ensemble of systems, the initial non equilibrium system must be a possible state and, therefore, will be represented. If we now define $\delta_i p$ as a delta function with a value one for micro states which have the desired properties of the original non equilibrium system and a value zero for all other states, the probability of a member of the equilibrium ensemble having the property is:

$$1\text{-}10 \qquad p_p = \sum p_i \, \delta_i p$$

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*The kinetic temperature of any system is defined by the following formula:

$$\frac{3}{2} n k T = \sum \frac{1}{2} m_i C_i^2$$

Where m_i is the mass of the ith atom and Ci is its velocity. k is the Boltzmann constant. This concept of temperature is derived from Chapman and Cowling (8). These authors note that "The kinetic-theory definition of temperature is applicable whether or not the gas is in a uniform or steady state; and, therefore, it provides a concept of temperature more general than that of thermodynamics and statistical mechanics, where only equilibrium states are considered."

The smaller the value of p_p, the more ordered the system. This accords with intuitive notions of order in that the equilibrium state is the state of maximum disorder consistent with the constraints. In measuring order, we compare states of equal temperature. The less probable a state is in its isothermal equilibrium ensemble the more ordered the system. In terms of classical statistical mechanics, the assertion is that ordered states of the system occupies regions of phase space far from the dense clusters characteristic of equilibrium in a canonical ensemble.

Since the pi are a normalized set of probabilities p_p is less than one. If we choose $-\ln p_p$ as our measure of order, it will always be positive and will increase as p_p decreases in accordance with our previous notions. By choosing this functional form, we also make contact with the formalism of information theory since $-\ln p_p$ is the amount of information we would have in knowing that a member of the equilbrium ensemble had the desired property of the initial non-equilibrium systems.

In defining order, we could have chosen our ensembles in alternative ways. The original non equilibrium system could have been adiabatically isolated at constant volume or isothermally and isobarically isolated. Each type of isolation leads to a different ensemble and corresponds to a different free energy function. The particluar isolation conceptionally employed is a matter of convenience although the numerical measure of order depends

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on the particular isolation used.

While $\sim p_i \ln p_i$ is the general case and $\sim p_i \ln p_i$ in the case of living systems are conceptually helpful as measures of order they suffer from the weakness that no direct experimental methods exist for getting at the quantities. However, a specific example yields some clues as to the relationships between our order measure and thermodynamically measurable quantities. Assume that p_i is zero for all i except one that is the non equilibrium system corresponds to only one state in the canonical ensemble. We may then write

1-11 $$p = \frac{e^{-\epsilon_i/kT}}{\sum_i e^{-\epsilon_i/kT}} = \frac{e^{-\epsilon_i/kT}}{Z}$$

where Z is the partition function of statistical mechanics.

1-12 $$-kT \ln p = \epsilon_i + kT \ln Z = A$$

where A = U - T S is the Helmholtz free energy. A may be regarded as the Helmholtz free energy of the non equilibrium state since ϵ_i =U and S = O as only one state comprises the system. -k T ln p is thus the fluctuation in Helmholtz free energy between the non equilibrium state and the equilibrium ensemble. The quantity $\sim \ln p$ is a ratio of stored energy (the difference in energy between the non equilibrium state and the equilibrium state) to thermal energy which turns out to be a useful parameter in the description of order. The class of functions used to

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designate order in this way will be referred to as L functions.

One further example extends the concept of order functions a bit further. Suppose that our initial isolation of the non equilibrium system were an adiabatic one at constant volume. The ensemble corresponding to this isolation is microcanonical in which all states have equal energy and equal a priori probability. Suppose, now, that there are a total of N possible states of the system and P of these possess the property of the initial non equilibrium system. Then:

1-13
$$\pi_p = \frac{P}{N}$$

1-14
$$-\ln \pi_p = -\ln P + \ln N$$

We may recast this in a thermodynamic form by noting that k ln N is the Boltzmann expression for entropy in a microcanonical ensemble.

1-15
$$-\ln \pi_p = -\frac{T_i \ln P}{T_i} + \frac{T_i \ln N}{k T_i}$$

1-16
$$-\ln \pi_o = -\frac{T_i \ln}{T_i} + \frac{T_i}{k T_i}$$

If we indicate by Si, k ln P the effective entropy of the initial configuration then -ln π_p is again the difference between two terms of the form of a configurational free energy divided by a thermal energy.

We may now generalize and summarize the case for isothermal isolation. First, note that on Page   , we have indicated the possibility

of defining a kinetic temperature for any system. We, now, assert that any

non equilibrium system can be completely described as a sub-ensemble of

the canonical ensemble having the same kinetic temperature volume and

chemical composition as the non equilibrium system. This is represented

in Figure 1-2. We can now pose the question: What is the probability of

finding a member of the canonical ensemble in the particular non equilibrium

configuration of interest? This is clearly:

$$1\text{-}17 \qquad p_{o} = \frac{\sum_{i} e^{-\epsilon_{i}/T}}{Z} = \frac{\sum_{i} e^{-\epsilon_{i}/kT} \, \delta_{i} \rho}{Z}$$

where the subscript   represents just those states that are members of

the non equilibrium subset. We can then define:

$$1\text{-}18 \qquad \Xi = \sum_{i} e^{-\epsilon_{i}/T}$$

$$1\text{-}19 \qquad A_{i} = -kT \epsilon_{i} + T \ldots \Xi \ldots$$

$$1\text{-}20 \qquad \Xi = \frac{e^{-\epsilon_{i}/T}}{\ldots}$$

We may then write:

$$1\text{-}21 \qquad \underline{\quad} = -q_{i} \delta \rho = \frac{A_{i} - A}{kT}$$

The order is represented by the fluctuation in Helmholtz free

energy necessary to specify the non equilibrium state divided by kT. At

equilibrium fluctuations of any appreciable magnitude are extremely rare. On the

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other hand, energy flow puts energy in the system and raises the probability

of occurrance of any given non equilibrium state.

In the preceeding discussion, we have implicity utilized the concept

of a complete set of chemical equilibrium states. Generally in thermodynamics

one uses state which are at equilibrium with respect to processes taking place

on one time scale, but which have not equilibrated with respect to processes

taking place at much slower rates. In the general formalism being discussed

here and in subsequent chapters on the evolution of biological systems, all

chemical processes must be considered. If one starts out, for example,

with a container of pure methane, the final equilibrium systems would include

all possible compounds of hydrogen and carbon. This type of complete

chemical equilibrium is, of course, much more difficult to deal with than

the more restricted equilibria which are usually treated. The ensembles

are considerably more generalized than those usually encountered in

statistical mechanics. This more general theory involves all the difficulties

of statistical treatment of pure species and simple mixtures plus a second

statistic over all possible molecular species. In subsequent chapters, we

will be concerned with attempts to treat this second statistic.

We now turn our attentions to the relation been ordering processing

and classical thermodynamics. The second law of thermodynamics demands

an increase of entropy accompanying any spontaneous process. The energy

flux thesis speaks of ordering of the intermediate system. Ordering is

usually thought to be associated with an entropy decrease so that we must

investigate the relation between the energy flux principle and the second law.

If we refer to Figure 1-3, we see a diagram of the generalized system

involved in energy flow considerations. The system may be split in two parts

the source - sink (s) and the intermediate system (i). The requirement of

the second law is that:

1-22
$$dS_s + dS_i \geq 0$$

The flow of energy from a source to a sink will always lead to an entropy

increase in the source sink system.

1-23
$$d\ Ss\ >\ O$$

The only restriction placed on d Si by the second law is:

1-24
$$-dS_i \leq dS_s$$

The entropy of the intermediate system may, therefore, decrease in an

energy flow process. In Chapter 5, we will discuss a somewhat more

generalized view of this problem from the point of view of local entropy

production.

We may make this idea more concrete by considering a model

system which involves such an entropy decrease. For the source and

sink consider two infinite isothermal reservoirs of temperature T_1 and T_2

where $T_1 > T_2$.   -22-

The intermediate system will consist of a Carnot engine driving a piston which is reversibly compressing M moles of perfect gas, which is thermostated by the lower temperature reservoir. In driving the engine around one complete cycle an amount of heat Q_1 is taken from the reservoir by the Carnot engine an amount Q_2 is given up to the sink and an amount of work W is done on the gas.

1-25
$$W = Q_1 - Q_2$$

In compressing the gas:

1-25A
$$W = -\int_{V_1}^{V_2} P\,dV = M R T_2 \ln \frac{V_1}{V_2}$$

Since the internal energy is a function of temperature only:

1-26
$$\Delta U = Q_3 - W$$

The amount of heat given to the reservoir Q_3 is equal to the amount of work done.

The entropy change of the source sink system is:

1-27
$$\Delta S_c = -\frac{Q_1}{T_1} + \frac{Q_2}{T_2} - \frac{Q_3}{T_2} = \frac{Q_3}{T_2}$$

Since $\triangle$ S for the Carnot engine is zero for one complete cycle, and is equal to $- Q_1/T_1 + Q_2 / T_2$.

For the gas in the piston.

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1-28 $$\Delta S_i = n \int \ldots V_{//} = -Q_3/T_2$$

The total entropy change

$S_t = Ss - Si = 0$ while the intermediate system is undergoing an

entropy decrease of Q_3 / T_2 .

Thus, we have shown that a spontaneous process may lead to a local

entropy decrease in an intermediate system between a source and a sink.

While the energy flow thesis is not derivable from the second law of thermo-

dynamics, it does not contradict this principle.

The previous discussion can be generalized by using the work principle

of Brönsted (9), Katchalsky and Curran (3) give the following statement of the

principle: "The over-all work ΔW performed by a system is the sum of

contributions due to transport of extensive quantities ΔKi across a difference

of conjugated potentials $i(1) - i(2)$

1-29 $$\Delta W = \sum_i \left(\mu_i - \mu_i \right) \Delta \Lambda_i$$

in which for example $i(1) - i(2)$ may be $T_1 - T_2$, $\ldots$

or $\ldots$ and the ΔKi will be ΔS, $\ldots$ or $\ldots$

respectively." T is temperature, is chemical potential, is

electrial potential, is mole number, and is electrial charge.

The $\not\sim i(1)$ and $\not\sim i(2)$ can be regarded as characteristic of the

source and sink. The transport of extensive quantities $\wedge Ki$ is always

accompanied by the flow of energy from source to sink. The reversible

flow of energy from source to sink across an intermediate system can always

give rise to a work term $\wedge W$. Part of this can always be used to order

the system. Hence, the generalized flow of energy from source to sink can

always lead to ordering of the intermediate within the restrictions of the

second law of thermodynamics.

In terms of our present view point, it is instructive to examine a

discussion of thermodynamics and life by Erwin Schroedinger (10). The

noted physicist raised the following point: "How would we express in terms

of the statistical theory the marvellous faculty of a living organism by which

it delays the decay into thermodynamic equilibrium (death)? We said before:

'It feeds upon negative entropy'. Attracting as if it were a stream of negative

entropy upon itself to compensate the entropy increase, it produces by living

and, thus, to maintain itself on a stationary and fairly low entropy level."

We may now reword the Schroedinger argument in the following

terms. An isolated organism will be subject to a series of processes tending

toward equilibrium. In statistical terms, it will tend to move from the very

improbable state that it is in to one of the very probable states associated

with the equilibrium ensemble. In order to prevent this drift toward equili-

brium, it is constantly necessary to perform work to move the system to the

improbable state that is the drifting out of. An isolated system, however,

cannot do steady work. The necessary condition for this is that the system be connected with a source and a sink and the work be associated with a flow of energy from source to sink. This flow will be an exentropic process in terms of the external world, i.e. the source and sink. When Schroedinger says that the organism feeds on negentropy, he means just that its existence depends on increasing the entropy of the rest of the universe.

While Schroedinger rather poetically worded his argument in terms of negentropy in the present analysis, we found it more useful to concentrate on the energy aspect of the argument. For non equilibrium systems, it is often difficult to define entropy while energy and energy flow are often more accessible quantities.

Interestingly, a very similar idea to the above was put forward by Otto Meyerhof (11). In a later series of lectures (12), he stated, "I advanced some time ago the general hypothesis that in consequence of the fluid state of the protoplasm and the instability of cell-stuffs, voluntary events of physical and chiefly of chemical nature are going on continuously which aim at a balance of the existing potentials of energy. Since life requires a continuation of these potentials of energy, work must be performed continuously for the prevention of reversion of these spontaneous changes". Again, we note that maintaining order requires continuous work, which can be supplied only by the flow of energy from a source to a sink.

Finally, we may note that the importance of energy flux in biology was grasped many tears ago by the physicist, Percy Bridgeman (13) whose penetrating analysis of thermodynamics included the remark, "For instance, the environment of most living things is a stream of radiation from the sun to the earth, from which they extract energy which is used in the 'organization' of the environment. The stream itself is a factor with order in the determining condition;".

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